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Medical and developmental risk factors of catatonia in children and adolescents: A prospective case–control study

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ABSTRACT

Context: Rare diseases have been associated with more and more genetic and non genetic causes and risk factors. But this has not been systematically assessed in catatonia, one of the psychiatric syndromes, that is most frequently associated with medical condition.
Objective: We sought to assess the medical and developmental risk factors of catatonia in children and adolescents.
Methods: From 1993 to 2009, 58 youths aged 10 to 18 years were prospectively admitted for catatonia and were followed up after discharge. A multidisciplinary approach assessed patients' medical condition and developmental history. A causality assessment scored medical risk (maximum score = 10; $\kappa = 0.91$). We compared the prevalence of catatonia in these patients to that of 80 inpatients with bipolar I disorder admitted from 1993 to 2003 who were also followed up.
Results: We found that 13 (22.4%) patients had medical conditions and 18 (31%) had a history of developmental disorder in the catatonia group, whereas 1 (1.3%) and 17 (22.6%) patients had the same conditions in the bipolar group ($p<0.001$; $p = 0.17$, respectively). Medical conditions associated with catatonia included auto-immune encephalitis (systemic lupus erythematosus [N = 3] and anti-NMDA-receptor encephalitis [N = 1]), seizures (N = 1), ciclosporin encephalitis (N = 1), post hypoglycaemic coma encephalitis (N = 1), and genetic or metabolic conditions (chorea [N = 2], 5HT cerebrospinal fluid deficit [N = 1], storage disease [N = 1], fatal familial insomnia [FFI; N = 1], and PRODH mutations [N = 1]). Six patients responded to a specific treatment approach related to their medical condition (e.g., plasma exchange in the case of auto-immune encephalitis).
Conclusion: Catatonia in children and adolescents is associated with a high prevalence of medical conditions. This needs to be acknowledged as it may greatly delay the treatment of catatonia and the diagnosis of medically related catatonia. Tragically, this may deny patients treatment opportunities.

1. Introduction

Catatonia is among the most severe psychiatric syndrome. The prevalence of catatonia in adult inpatients ranges from 7.6% to 38%. Catatonia is more frequent among women and its most commonly associated psychiatric diagnosis is mood disorder (Taylor and Fink, 2003). Catatonia has not been fully investigated in children and adolescents, although it can occur in children and adolescents. In this age group, catatonia is rare, and it increases the risk of premature death (including suicide) by 60-fold, making it the most severe psychiatric condition (Cornic et al., 2009). The prevalence of catatonia in children and adolescent inpatients is estimated to range from 0.6% to 17.7% according to different inclusion criteria (e.g., general psychiatric unit vs. adolescents receiving electroconvulsive therapy (ECT); high income vs. low income country inpatient unit) (Cohen et al., 2005). In contrast to adult catatonia, catatonia in children and adolescents is more frequent in boys than in girls (Cohen et al., 2005; Thakur et al., 2003). The most commonly underlying psychiatric disorder is schizophrenia (Cohen et al., 2005; Takaoka and Takata, 2003), but it can also occur in youths with a history of developmental disorder (e.g.,

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pervasive developmental disorder [PDD] or intellectual disability [ID]) (Dhossche et al., 2006; Wing and Shah, 2000). Gender difference between paediatric and adult catatonia can be explained by gender differences in underlying psychiatric disorders (early onset schizophrenia is more frequent in boys and mood disorders are more frequent in women). However, the clinical presentation of paediatric catatonia is similar to that in adults, which involves psychological symptoms (e.g., mutism and social withdrawal) and motor symptoms (e.g., stupor and waxy flexibility). These symptoms can be continuous or discontinuous. Symptomatic treatments are also similar to that in adult catatonia. The first line of treatment is high doses of benzodiazepines (e.g., lorazepam ≤ 15 mg/day). In cases of resistant or malignant catatonia, electroconvulsive therapy (ECT) is recommended, even in patients with PPD or ID (Taylor and Fink, 2003; Wachtel et al., 2008). In addition, clinical practice depends on the possibility of curing the underlying condition. Indeed, catatonia may occur in patients with various psychiatric disorders (usually schizophrenia and severe mood disorders) and medical conditions (e.g., neurological conditions, intoxication, auto-immune diseases, and metabolic conditions) (Cottencin et al., 2007; Lahutte et al., 2008). Some of these conditions have poor prognoses and may result in death (Dimitri et al., 2006). Recognising underlying medical conditions is essential because it may lead to a cure. Given the variety of possible medical conditions, guidelines have been proposed to help clinicians challenged by this complex issue (Lahutte et al., 2008).

Since 1993, we prospectively followed up a sample of youths with catatonia to investigate their socio-demographic characteristics, symptomatologies, psychiatric and medically associated conditions, developmental histories and outcomes (Cohen et al., 1999; Cohen et al., 2005; Cornic et al., 2009). This study aimed to: (1) assess the prevalence of medical risk factors and developmental histories in this sample of patients with catatonia; (2) compare it with the prevalence of medical risk factors and developmental histories found in a sample of inpatients with bipolar I disorder; and (3) assess whether socio-demographic or clinical characteristics help distinguish catatonia associated with medical/developmental risk factors from catatonia with no such risks.

2. Methods

2.1. Patient recruitment

We assessed all patients admitted to the Department of Child and Adolescent Psychiatry at University Hospital La Pitié-Salpêtrière between 1993 and 2009 for catatonia. In all, we hospitalised 5532 patients aged 4 to 18 years. To obtain a diagnosis of catatonia, patients must present at least two motor symptoms or one motor symptom and a non-motor symptom indicative of severe behavioural and emotional impairment. The catatonia symptom list (see Supplementary Table 1) was based on the modified version of the Bush and Francis scale (Bush et al., 1996; Cohen et al., 1999; Cohen et al., 2005; Ey, 1950). We excluded patients who presented extrapyramidal syndrome secondary to antipsychotic symptoms from participation. Recruitment details are available in previous publications (Cohen et al., 2005; Cornic et al., 2007; Cornic et al., 2009). During the inclusion period, previous reporting created more attention and interest for the syndrome leading to a higher frequency of recruitment due to transfer from other French units after 2006 (40 vs. 18 inclusions, respectively). This corresponds to the opening of the French National Centre for Psychiatric Rare Diseases and Catatonia in the Department of Child and Adolescent Psychiatry at University Hospital La Pitié-Salpêtrière. We included 58 patients in this sample, aged from 9 to 18 years. Follow up clinical data of a sub-sample have been previously published (Cornic et al., 2009). Here we focused on medical conditions and developmental history.

We compared patients' prevalence of medical conditions and their developmental histories to those of a control sample of 80 inpatients with type I bipolar disorder (BP) hospitalised in the same department between 1993 and 2003. We followed up this sample between 2005 and 2006. Brunelle et al. provide a detailed description of the control sample (Brunelle et al., 2009). Forty-nine (61.3%) control youths were hospitalised for a manic episode; 31 (38.7%) was hospitalised for a mixed episode. We excluded 5 patients from the control group because they had a catatonic episode associated with BP. The local Ethics Committee approved this study.

2.2. Patient assessment

We conducted a systematic assessment within the patients' first week of admission, and repeated this assessment at discharge and follow-up. This assessment included: (i) socio-demographic data (age, sex, origin and family social-economic status; SES); (ii) a semi-structured interview to evaluate patients' personal and family histories of psychiatric and medical disorders (detailed in (Taieb et al., 2002)); (iii) a clinical examination; (iv) the modified version of the Bush and Francis scale to test for the presence and severity of catatonic symptoms (Bush et al., 1996; Cohen et al., 1999; Cohen et al., 2005; Ey, 1950); (v) the Clinical Global Impression—Severity scale (CGI-S) (Guy, 1976) and the Global Assessment Functioning scale (GAF) to assess patients' clinical severity at admission and discharge; and (vi) the duration of the psychiatric episode, the duration of hospitalisation, the type of catatonia onset (e.g., <10 days = acute; ≥10 days = insidious), the duration of acute catatonia, and the type of catatonia (e.g., episodic or chronic). We considered catatonia as chronic if the patient had catatonic symptoms after discharge from the index episode. All but 7 patients had a follow up visit at least 6 months after discharge assessment (Endicott et al., 1976).

We diagnosed psychiatric conditions associated with catatonia according to DSM-IV criteria. The Diagnostic Interview for Genetic Studies (DIGS) version 2.0, a semi-structured diagnostic interview developed by the Human Genetics Initiative of the National Institute of Mental Health, assessed lifetime and current psychiatric diagnoses (www.nimhgenetics.org; French translation by CL) (Nurnberger et al., 1994). The DIGS elicits information necessary to diagnose psychotic, mood, anxiety, substance use and eating disorders as well as suicidal behaviours using the DSM-IV criteria. We interviewed most patients after the acute phase of their illness. To maximise the accuracy of our psychiatric diagnoses, we obtained clinical information from each patient's regular psychiatrist. Based on all available information, the consensus reached by the patient's treating clinician, the DIGS interviewer and one additional child/adolescent psychiatrist (DC or AC) diagnosed patients. In cases of ID or PDD, we confirmed diagnoses using the parental Autism Diagnostic Interview—Revised (Lord et al., 1994) and the Wechsler Intelligence Scales. Both scales are used routinely in the department. If we confirmed an ID or PDD diagnosis, a geneticist performed a systematic clinical and molecular evaluation including karyotype and search for 22q11 and 15q11–q13 chromosomal abnormalities by FISH in all patients, and search for Fragile X in boys (if the patient had never had this procedure performed).

2.3. Medical condition search

To maximise the accuracy of medical diagnoses, an internist and a neurologist performed an additional physical examination on all patients. In previous reports, we proposed guidelines for clinical and para-clinical investigations to help determine the medical conditions associated with catatonia (Lahutte et al., 2008; Sedel et al., 2007). Determining a medical condition from somatic and psychiatric examinations does not occur immediately because pathognomonic symptoms are rare and catatonia is occasionally isolated. Some symptoms must be actively searched for to orient a diagnosis. We used a multidisciplinary approach with the same medical staff during follow-up. Neurological, global examinations and psychiatric assessments were performed to